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10/642,615	08/19/2003	Ali Afzali-Ardakani	YOR920030023US1	3761	
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SUITE 200 VIENNA, VA 22182-3817		ART UNIT	PAPER NUMBER		
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

	Application No.	Applicant(s)			
	10/642,615	AFZALI-ARDAKANI ET AL.			
Office Action Summary	Examiner	Art Unit			
	Yelena G. Gakh, Ph.D.	1743			
The MAILING DATE of this communication app Period for Reply	ears on the cover sheet with the c	orrespondence address			
A SHORTENED STATUTORY PERIOD FOR REPLY WHICHEVER IS LONGER, FROM THE MAILING DA - Extensions of time may be available under the provisions of 37 CFR 1.13 after SIX (6) MONTHS from the mailing date of this communication. - If NO period for reply is specified above, the maximum statutory period w - Failure to reply within the set or extended period for reply will, by statute, Any reply received by the Office later than three months after the mailing earned patent term adjustment. See 37 CFR 1.704(b).	ATE OF THIS COMMUNICATION 36(a). In no event, however, may a reply be tim vill apply and will expire SIX (6) MONTHS from a cause the application to become ABANDONE	N. nely filed the mailing date of this communication. D (35 U.S.C. § 133).			
Status					
1) Responsive to communication(s) filed on 20 Ju	<u>ıne 2007</u> .				
2a) This action is FINAL . 2b) ⊠ This	This action is FINAL . 2b)⊠ This action is non-final.				
3) Since this application is in condition for allowar	☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is				
closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11, 453 O.G. 213.					
Disposition of Claims					
4) ⊠ Claim(s) 1-19 is/are pending in the application. 4a) Of the above claim(s) is/are withdray 5) □ Claim(s) is/are allowed. 6) ⊠ Claim(s) 1-19 is/are rejected. 7) ⊠ Claim(s) 19 is/are objected to. 8) □ Claim(s) are subject to restriction and/or	vn from consideration.				
Application Papers					
9) The specification is objected to by the Examine 10) The drawing(s) filed on is/are: a) access applicant may not request that any objection to the Replacement drawing sheet(s) including the correct 11) The oath or declaration is objected to by the Ex	epted or b) objected to by the lead of the drawing(s) is object of the lead of	e 37 CFR 1.85(a). jected to. See 37 CFR 1.121(d).			
Priority under 35 U.S.C. § 119					
 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f). a) All b) Some * c) None of: 1. Certified copies of the priority documents have been received. 2. Certified copies of the priority documents have been received in Application No. 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)). * See the attached detailed Office action for a list of the certified copies not received. 					
Attachment(s) 1) Notice of References Cited (PTO-892) 2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date	4) Interview Summary Paper No(s)/Mail Da 5) Notice of Informal P 6) Other:	ate			

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DETAILED ACTION

1. This action is issued in accordance with the Panel Decision from Pre-Appeal Brief Review on 06/20/07. The prosecution is re-opened and an additional rejection over the prior art is established for the pending claims 1-19. Objection to the specification and rejection of the pending claims under 35 U.S.C. 112, first paragraph, remains.

The examiner re-considers the subject matter of the pending claims in two ways - first, as the recitation of the molecular manipulator as disclosed in the specification, i.e. the molecule, which is capable of acting as tweezers because of changes in its steric structure; and second, as the recitation of the light-sensitive molecule attached to the probe, irrelevant of its function. As demonstrated by the examiner below, the claims considered in the first way are rejected as not being enabled by the specification, since the specification does not enable using the molecules recited in the claims as molecular manipulators, not mentioning the hypothetical nature of the molecules. The claims considered in the second way are rejected over the prior art, since the prior art discloses light-sensitive molecules, specifically azo-molecules undergoing cis-trans isomerism under UV radiation, attached to the probe.

Response to Amendment

2. Amendment filed on 03/19/07 has been entered. Claims 1-19 are pending in the application.

Specification

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to as not enabling the use of the hypothetical molecules disclosed in the specification as the molecular manipulator. The disclosure describes in general terms the Applicants' hypothesis for a possible molecular manipulator, without any evidence for enabling the Applicants' hypothetical molecule. The molecules depicted on Figures 1 and 2 are not CA registered (the library search report is attached) and obviously do not exist. The

Applicants did not provide any possible synthetic path for obtaining such molecules, not mentioning their testing as molecular manipulators. The hypothesis is not experimentally proven. The structure indicated as an example cannot be used as a manipulator as disclosed in the specification, since it would have a highly non-planar structure, contrary to what is depicted in the drawings. Moreover, its steric configuration and energetic state would not provide conditions favorable for using such molecules as manipulators as can be clearly seen from the prior art described below.

Claim Objections

4. Claim 19 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Since there is always a space between the two arms, the subject matter of claim 19 does not further limit the recitation of the parent claim.

Claim Rejections - 35 USC § 112

- 5. The following is a quotation of the first paragraph of 35 U.S.C. 112:
 - The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
- 6. Claim 9 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Diazo-compounds comprise a moiety -C=N=N-, which is linear, and therefore no cis-trans-isomers exist for such molecules.
- 7. Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Breath of the Claims

The claims recite in the most general terms "a molecule manipulator" comprising a light-sensitive molecule with a double bond, in particular azo-bond, which changes its configuration upon light irradiation, with the molecule attached to the probe of a scanned-proximity probe microscope. No specifically synthesized molecules, which can act as molecular manipulators as recited in the claims, are disclosed in the specification. Two examples depicted on the pictures are not the real molecules and are not enabled as the molecular manipulators. The specification does not provide any guidance for their synthesis or any evidence of their ability to act as molecular manipulators.

The Nature of the Invention

The invention is directed toward a hypothetical molecular manipulator based on a known fact of cis-trans light-induced transformation of azo-bond. The hypothetical molecules are attached to the tip of the atomic force microscope (AFM). Two molecules are depicted on Figures 1-2 as the examples. The molecules are not known in the literature and do not have CA registration numbers (the library search report is attached). They are not described in the specification as the known molecules; however, their synthesis is not provided either. Even if the molecules were synthesized, they would not be enabled as molecular manipulators, since they would have highly non-planar structures with a restricted rotation of benzene fragments about the diphenyl bondm, which do not meet specific geometric requirements for molecules to be molecular manipulators. The prior art does not provide any basis for any expectation of success for the claimed invention, as demonstrated below.

The State of the Prior Art

The prior art is in the field of nanotechnology related to "molecular machines" or "molecular tools". The examiner searched patent and non-patent literature pertinent to molecular tweezers, clips, manipulators, motors, etc. One of the most recent papers on molecular motors, "Molecular Motor Spins On Surface" by Netherlands chemists was proclaimed as the "first light-driven molecular rotary motor attached to a solid surface" (Chemical & Engineering News, 2005): "by anchoring a chiral helical alkene onto a gold nanoparticle, chemists in the

Netherlands have created the first light-driven molecular rotary motor attached to a solid surface (Nature 2005, 437, 1337). This mounted molecule, the researchers say, "might be a first step toward the construction of more elaborate and functional nanosized mechanical devices" and perhaps systems to exploit solar energy. Fastening a rotary molecule to something solid, as Ben L. Feringa and colleagues at the University of Groningen have done, brings these spinning systems closer to becoming useful nanomachines. Putting motors on a surface is important because it should make it easier for them to do useful things, like move themselves or cargo, or change the nature of the surface in response to a stimulus," says T. Ross Kelly, a Boston College chemistry professor who made a molecular motor that runs on chemical fuel. Feringa's team uses two thiol groups to affix their molecular motor to a gold nanoparticle. Two eight-carbon legs link these thiols to the alkene motor. The researchers note that they chose this lengthy anchor to minimize any direct electronic interaction between the alkene and the gold particle. The researchers start the motor's rotation by photoisomerizing the double bond. This forces the methyl group on the molecule's lone stereocenter into an energetically disfavored orientation. When heated, this unstable isomer undergoes a helical inversion, resulting in a net 180° rotation. This step also ensures unidirectional movement. Repeating the two isomerizations completes the 360° revolution". The molecules have extremely well defined steric structure with experimentally proven behavior as molecular manipulators.

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Klärner et al. (Acc. Chem. Res., 2003) provide a detailed review of "Molecular Tweezers and Clips as Synthetic Receptors" with tweezers and clips containing naphthalene and benzene spacer units, which are synthesized by repetitive Diels-Alder reactions. The tweezers and clips should possess specific structural, thermodynamics and other physical-chemical requirements in order for such host-guest interaction to take place: "these molecules are well pre-organized because of their belt-type structures. But bond angle distortions require lithe energy and, therefore, should induce certain flexibility in these systems, allowing the receptor "arms" to be expanded and compressed during the substrate complexation in a way comparable to the working principle of mechanical tweezers. Thus, a fit of the receptor geometry to the substrate topography to a certain extent, induced by the complex formation, can be expected. The size and shape of the receptor cavities can be systematically varied by varying the number and size of the spacer units. Finally, the parent compounds la-Ta are simple hydrocarbons containing only nonconjugated

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benzene and/or naphthalene rings arranged in a belt-like concave- convex topography, so that an aromatic substrate can be bound via multiple π - π and CH- π interactions" (page 920).

Feringa et al. (Appl. Phys., 2002) describe "Light-driven molecular switches and motors" with detailed disclosing of physical-chemical properties of molecular motors comprising double bond, which undergoes light-induced cis-trans transformation. Specific requirements should be fulfilled for the switches and motors to perform their functions. Jones et al. and Pearson et al. (J. Org. Chem., 1997) described in detail "Molecular scale wires with alligator clips" providing their full synthesis and physical-chemical characteristics. A series of papers is devoted to molecular devices based on light-induced cis-trans transformation of azo-bond in azobenzene moieties. Stiller et al. (Surface and Interface Analysis, 2000) teach "scanning Kelvin microscopy as a tool for visualization if optically induced molecular switching in azobenzene self assembling films"; Hugel et al. (Science, 2002) disclose "single-molecule optomechanical cycle" with a detailed study of molecular devices based on photosensitive azobenzene polymers. Muraoka et al. (J. Am. Chem. Soc., 2003) describe "light-driven open-close motion of chiral molecular scissors" based on azobenzene expansion and contraction (cis-trans transformation) of N=N bond. Jousseime et al. (J. Am. Chem. Soc., 2003) teach "photomechanical actuation and manipulation of the electronic properties of linear π -conjugated systems" using azobenzene chromophore. Wen et al. (J. Phys. Chem. B, 2005) teach "photochemical-controlled switching based on azobenzene monolayer modified silicon (III) surface". Bellini et al. (J. Phys.:Condens. Matter, 2006) disclose "light-induced molecular motion of azobenzene-containing molecules: a random-walk model". None of the recited papers indicate the possibility of using molecules recited in the claims and those depicted on Figures 1 and 2 as molecular manipulators; the examiner did not find any reference, which would disclose a synthesis of similar compounds. The bulkiness of the cis-conformer of a hypothetical structure 1A would assume its high nonplanarity, which would totally prevent its ability to grab molecules and be used as a molecular manipulator.

The Level of One of Ordinary Skill

The examiner considers synthesis of any of the hypothetic structures disclosed in the specification, including those depicted on Figures 1 and 2 and recited in the claims beyond the skill of a routineer in the art until the Applicants prove otherwise. Moreover, even in the case of

successful synthesis of such structures, it is outside the scope of any routineer in the art to study these molecules in relation to their ability to be molecular manipulators, as demonstrated by highly complex and detailed studies of molecular tools disclosed in the prior art.

The Level of Predictability in the Art

The prior art does not provide any ground for any reasonable expectation of success in using hypothetical structures disclosed in the specification as molecular manipulators.

The Amount of Direction Provided by the Inventor

The instant disclosure does not provide any direction neither to the synthesis of the hypothetical structures disclosed in the specification, nor to their application as molecular manipulator.

The Existence of Working Examples

No working examples are provided by the specification for either the synthesis of the compounds disclosed in the specification and their attachment to the microscope probe, or for their application as molecular manipulators, which would require rigorous studies of their spatial structure and physical-chemical characteristics, such as enthropy and enthalpy changes, for their application as molecular manipulators.

The Quantity of Experimentation Needed to Make or Use the Invention Based on the Content of the Disclosure

It requires an undue experimentation to synthesize hypothetical compounds disclosed in the specification and even more undue experimentation to study them as potential molecular manipulators.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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9. Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "a probe to which the light-sensitive molecule is attached". "A probe" is not a definite term of the art. The term "probe" has multiple meanings, most of which could read on the subject matter of the claim. The probe can be a chemical probe for a target molecule, which is tagged with the light-sensitive compound comprising a double bond. It can be a physical surface, to which the light-sensitive compound is attached as a photo-sensitive coating. The term "probe" renders the claim unclear and indefinite regarding the scope of what is claimed.

In claim 2 it is not clear, what is "a line" of a scanned-proximity probe microscope, and how can the light-sensitive molecule be attached to the line?

In claim 5 it is not apparent as what is "a moiety located between the two arms"? Is this the central part of the molecule between two arms? Since the molecule is supposed to work as molecular tweezers, the claim can be interpreted as reciting the light-sensitive molecule holding the chemical moiety between its arms.

The meaning of claim 10 is not clear. What does the following expression mean: "an azo double bond having the same cis-trans configuration, when illuminated by the light of the selected wavelength"? This phrase does not make much sense. First, it is not clear as to how the double bond can have cis-trans configuration? It can have either cis-, or trans-configuration. Also, it is not apparent as to why having cis-trans configuration depends on illuminating the double bond by the light? Double bonds always possess either cis- or trans-configuration, independent on any illumination with the light. If the claim was supposed to recite simultaneous *changes* in cis- or trans- configuration in both arms upon illuminating by the light, then this should be clearly recite in the claim.

Claim 19 obviously does not recite any further limitation to the parent claim.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-8, 11-16 and 18-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Stiller et al. (Surface and Interface Analysis, 2000).

Stiller discloses a light-sensitive azo-benzene derivative with two arms, one of which includes the double bond -N=N-, which undergoes cis-trans isomerization upon illuminating with UV light, and the other one is different from -N=N- - bond (Figure 1), attached to the scanning force microscopy (SFM) probe, which conventionally comprises any of silicon, silicon oxide, aluminum oxide or titanium oxide (claims 1-7). Since the moiety recited in the claims does not have a definite and clear interpretation and can be interpreted in various way, the examiner considers the phenyl ring to be such moiety (claim 11). The functional group R is CF₃ (a haloalkyl) (claim 12). The molecule is covalently bound to the probe through SH-group (claims 13-14). The probe is coated with gold (claim 16). The arms have different lengths (claim 18) and a space between them (the whole molecular fragment between them).

12. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Hugel et al. (Science, May 2002).

Hugel discloses a light-sensitive polymer comprising azobenzene units attached to atomic force microscope (AFM) probe comprising Flint glass.

Claim Rejections - 35 USC § 103

- 13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
 - (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
- 14. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

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1. Determining the scope and contents of the prior art.

- 2. Ascertaining the differences between the prior art and the claims at issue.
- 3. Resolving the level of ordinary skill in the pertinent art.
- 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
- 15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).
- 16. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stiller.

While Stiller discloses a commercially available compound comprising one azo-group, it would have been obvious for any person of ordinary skill in the art to introduce the second azo-group to enhance the effect of the azo-compound attached to the SFM probe.

17. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stiller in view of the prior art disclosed by Nakagawa (US 5,353,632).

While Stiller does not specifically disclose coating comprising trichlorosilane, Nakagawa describes such coating as being conventional and disclosed in the prior art: "the other insulation comprises octadecyl-trichlorosilane (OTS)" (see Background of the Invention, col. 1, line 56). Therefore, it would have been obvious for any person of ordinary skill in then art to apply OTS coating indicated by Nakagawa to the probe disclosed by Stiller as an additional protection layer with an obvious modification of the moiety of the azo-compound to covalently bind to the coating, which would be within the skill of a routineer in the art.

Response to Arguments

18. Applicant's arguments filed 03/19/07 have been fully considered but they are not persuasive.

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The Applicants indicate: "Applicants again submit that the test for enablement is "whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention." (See M.P.E.P. § 2164.01; emphasis added by Applicants)". The examiner totally agrees with this MPEP recitation. However, the examiner disagrees with the Applicants' position that their disclosure meets the criteria of this test. Not only the examiner indicates that the Applicants' disclosure is hypothetical, which it is, but also that it does not provide any basis for enabling the disclosed hypothetical structure as molecular manipulators. Regarding prophetic or any other examples, MPEP (2164.02) clearly states: "when considering the factors relating to a determination of non-enablement, if all the other factors point toward enablement, then the absence of working examples will not by itself render the invention non-enabled. In other words, lack of working examples or lack of evidence that the claimed invention works as described should never be the sole reason for rejecting the claimed invention on the grounds of lack of enablement". The examiner has clearly demonstrated why the instant invention is not enabled, by providing all eight criteria for evaluating enablement of the invention. The invention is not enabled according to all eight criteria, rather than just a lack of the working example.

Regarding the Applicants' statement that "the Applicants submit that the experimentation required by one skilled in the related art to make and use the claimed invention is clearly routine (as is illustrated in the documents submitted in the Information Disclosure Statement filed on August 19, 2003)", the examiner respectfully requests the Applicants to explain, how three reference submitted in said IDS, namely: a, "Supramolecular Chemistry", disclosing rigid highly conjugated polyaromatic compounds, b, research project related to molecular tweezers based on p-stacking of DNA molecules, and c, the paper describing properties of polymethylene-linked bisviologens-2-naphthol complexes, are related to the compounds of the instant application and their use as molecular manipulators. The examiner did not find in the provided IDS any structure related to azo-compounds, less so using azo-compounds as molecular manipulators. If the examiner misses some information from the references provided by the Applicants, the examiner respectfully requests the Applicants to specifically indicate, where the references disclose the subject matter related to the instant application.

Next Applicants' statement is quite puzzling. First the Applicants state that the experimentation required to make and use the claimed invention is clearly routine, and then immediately they indicate that "the degree of experimentation that is considered routine is also high". The experimentation can be either routine, or of a high level. These definitions are mutually excluding. If the experimentation that is required for practicing the invention is high, the disclosure should provide detailed description of the invention along with the working examples.

Regarding 112, second paragraph, rejection, the examiner would like to indicate that, according to MPEP 2173: "the primary purpose of the requirement of definiteness of claim language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent". The term "probe" has a plurality of meanings, with a plurality of possible interpretations applicable to the subject matter of the claims. For example, a biological probe, which may be a biomolecule, such as protein or DNA, can read on the recitation of claim 1, since such probes are known to be tagged with photosensitive compounds. The probe can be just a substrate, which can be coated with the photo-sensitive compound. A plurality of possible interpretation of the term conventional in different areas of the field leads to multiple interpretations of the scope of the invention, which renders the claims unclear and indefinite.

Regarding claim 5 and Applicants' referring to drawings 1 and 2 as an explanation of the term "moiety", the examiner is not quite sure, as to which "moiety" the Applicants are talking about. The examiner respectfully requests the Applicants to name the moiety, which for example is depicted on Figures 1 and 2.

Regarding claim 10, the examiner did not understand the meaning of the claim and tried to provide the Applicants with her own interpretation of the claim. In response the examiner expected the Applicants to either confirm the interpretation of the claim provided by the examiner, or explain it further. The Applicants did neither, and the meaning of claim 10 remains obscure to the examiner.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

07/30/07

YELENA GAKH PRIMARY EXAMINER